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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/757,505	01/15/2004	Caroline Delattre	016800-583	6320

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EXAMINER	
FERNANDEZ, SUSAN EMILY	
ART UNIT	**PAPER NUMBER**
1651	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/22/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/757,505	DELATTRE ET AL.	
	Examiner	Art Unit	
	Susan E. Fernandez	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,9-11,13,14,16,17,21,24,25,27-29,33 and 35-60* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,9-11,13,14,16,17,21,24,25,27-29,33 and 35-60* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed December 22, 2006, has been received and entered.

Claims 2-8, 12, 15, 18-20, 22-23, 26, 30-32, and 34 are cancelled. Claims 43-60 are new.

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, 33, and 35-60 are pending and examined on the merits to the extent they read on the elected subject matter and species. The species election in the replies filed on February 23, 2005 and February 24, 2006 apply to the amended claims (for instance, election of aspartylglucosaminidase, now recited in claims 1, 24, 25, 27-29).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, 33, and 35-51 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Specifically, the invention encompasses a regime/regimen comprising the topical application of at least one hydrolase polypeptide having amidase activity selected from the group consisting of aspartylglucosaminidase, glutaminase, amidase, urease, aminoacylase, aspartolacylase, ceramidase, peptidyl-glutaminase, formamidase, and pentanamidase, and any

and all activators of said hydrolase polypeptide. However, the specification only discusses the use and the prodesquamating effect of aspartylglucosaminidase (AGA) (page 28, paragraph [00137]), and the applicant has not demonstrated that each of these recited hydrolase polypeptides have the required effects as recited in the preamble of the claims (regime/regimen for promoting desquamation of the skin and/or for promoting hydration of the skin, etc.). Thus there is only written description for aspartylglucosaminidase (AGA).

Similarly, the specification only indicates sodium dodecyl sulphate (SDS) and sodium lauryl ether sulphate as activator of a hydrolase polypeptide having amidase activity (page 11, paragraph [0050]), and does not describe any other compounds appropriate for activating the polypeptide. Thus, a holding of lack of written description is clearly required

Applicant's arguments filed December 22, 2006, have been fully considered but they are not persuasive. Though applicant has further limited the hydrolase polypeptide to those now recited in claim 27, the examples of the specification as filed do not demonstrate that each and every one of these polypeptides promote desquamation of the skin and/or promote hydration of the skin. Moreover, the listed hydrolase polypeptides have very different activities and result in different products following hydrolysis. For instance, McGovern et al. (Journal of Biological Chemistry. 1983. 258(17): 10743-10747) teaches that aspartylglucosaminidase (AGA) hydrolyses N-acetyglucosamine-asparagine linkages (page 10743, first line). On the other hand, another of the recited hydrolase polypeptides, urease, is disclosed as catalyzing the hydrolysis of urea to ammonia and carbonic acid (see page 6492, first paragraph of "Discussion," Young et al., Journal of Bacteriology, 1996, 178(22): 6487-6495). Clearly, the polypeptides recited in the claims act on different compounds which thereby result in different products. Therefore, these

hydrolase polypeptides must act differently on the skin and so it is unclear that each and every one of the recited hydrolase polypeptides promote desquamation and/or hydration of the skin. The specification does not teach that each and every one of these recited hydrolase polypeptides, despite their different activities, would result in the claimed effects on the skin. Thus, the rejection concerning written description for the hydrolase polypeptides used is required.

With respect to the written description requirement concerning the activator for the hydrolase polypeptide, though the applicant correctly points out that sodium dodecyl sulphate and sodium lauryl ether sulphate are described as suitable activators in the specification, paragraph [0047] does not provide sufficient description to convey to one skilled in the art that the inventors had possession of the claimed invention with respect to the activator. Paragraph [0047] provides insufficient support since it does not describe how these activators stimulate the activity of each and every one of the recited hydrolase polypeptides. Moreover, M.P.E.P. §2163 teaches that there is sufficient description if "the written description adequately links or associates adequately described particular structure, material, or acts to the function recited in a means- (or step-) plus-function claim limitation", or if "it is clear based on the facts of the application that one skilled in the art would have known what structure, material, or acts perform the function recited in a means- (or step-) plus-function limitation". The instant disclosure does not meet either of these criteria as the skilled artisan would not be able to determine which compounds do or do not perform the claimed function (activation of hydrolase polypeptides) without extensive experimentation. Thus, the written description rejection must be maintained for any activator other than sodium dodecyl sulphate and sodium lauryl ether sulphate.

Claims 43-60 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Regarding undue experimentation, *In re Wands*, 8 USPQ2d 1400, at 1404 (Fed. Cir. 1988) states:

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized by the board in *Ex parte Forman*. They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. (Citations omitted).

Claims 43-60 indicate that the "activator" of the elected hydrolase polypeptide, aspartylglucosaminidase (AGA), is sodium dodecyl sulfate (SDS) or sodium lauryl ether sulfate. However, it is unclear that either of these two compounds increase the rate of the enzymatic reaction of aspartylglucosaminidase, or any other hydrolase polypeptide having amidase activity. No working examples are provided in the specification that show that SDS or sodium lauryl ether sulfate increase the activity of AGA or any other hydrolase polypeptide for that matter. Moreover, Enomaa et al. (Biochem. J. 1992. 286: 613-618) observes the effects of SDS on AGA activity at various temperatures and SDS concentrations (page 613, last paragraph through page 614, first paragraph). Figure 3 on page 614 of Enomaa et al. compares the activity of AGA in the absence or presence of SDS, and it is evident that for every temperature and concentration of SDS tested, the presence of SDS decreases the activity of AGA. Therefore, the prior art clearly teaches that SDS is clearly not an "activator" of AGA.

Because of the lack of working examples and the state of the prior art, the application is not enabled for SDS or sodium lauryl ether sulfate as "activators" of aspartylglucosaminidase or any other hydrolase polypeptide.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 9-11, 13, 14, 16, 17, 21, 24, 25, 27-29, 33, and 35-42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fein (US 2003/0026794) in view of Baumann et al. (Biochem. J. 1989. 262: 189-194).

Fein discloses a method "...for treating a patient having a condition involving the epidermal, and/or dermal, and/or subcutaneous layer of skin using a composition containing at

least one enzyme that affects one or more particular layers of skin" (page 1, paragraph [0008]). As the methods taught in Fein are for treating hyperkeratotic disorders wherein normal desquamation does not occur, such as xerosis (dry skin) (page 3, paragraphs [0029] and [0034]), a regime or regimen for promoting desquamation of the skin and/or for promoting hydration of the skin is taught, as required by instant claims 1, 24, and 27. Since a regime or regimen for promoting desquamation/hydration of skin is taught, regimen for promoting cicatrisation (instant claim 25), facilitating the penetration into the skin of a cosmetic/dermatological active agent (instant claim 28), and combating bacterial adhesion to the skin (instant claim 29) are also taught. The Fein invention teaches the topical application of enzymes (abstract), where the enzymes may be amidases or ceramidases (page 3, paragraph [0042]) which are actually recited as hydrolase polypeptides having amidase activity in the pending claims, but were not elected for examination. The enzymes are delivered in a suitable, physiologically acceptable formulation (page 5, paragraph [0053]) in an amount which can range from about $1x10^{-9}$ % w/v to about 80% w/v of the formulation (page 2, paragraph [0010]). Thus, limitations recited in instant claims 1, 9-11, 13, and 14 are taught by the reference.

The enzyme formulation of the Fein invention "...may also contain other compounds that have desirable therapeutic, cosmetic, and/or aesthetic properties, that either do not affect or only minimally affect the activity of the enzyme" (page 5, paragraph [0054]). Alpha-hydroxy acids, EDTA, a moisturizing cream base, and exfoliants (thus permeating agent) may be included in the enzyme formulation (page 5, paragraph [0054]). Therefore, limitations of claims 16 and 17 are taught (EDTA is a desquamating agent).

Fein differs from the claimed invention in that it does not teach that the hydrolase enzyme topically applied to the skin is the elected enzyme, aspartylglucosaminidase. Furthermore, Fein does not teach that the enzyme formulation further comprises at least one "activator" of the hydrolase enzyme.

Baumann et al. discusses human aspartylglucosaminidase (AGA), an enzyme known to hydrolyze beta-aspartylglycosylamine linkages (page 189, first paragraph). For purified AGA, the effect of pH on enzymatic activity was determined with various buffers (page 192, last paragraph through page 193, first paragraph). As Figure 5 on page 193 demonstrates, the enzyme activity was most optimal at a pH of about 6, where the buffer used at this pH is a citrate/phosphate buffer.

At the time the invention was made, it would have been obvious to the person of ordinary skill in the art to have used aspartylglucosaminidase as the hydrolase enzyme of the Fein enzyme formulation for treating skin. One of ordinary skill in the art would have been motivated to do this since there would have been a reasonable expectation of success in substituting one hydrolase for another. Furthermore, Fein does not limit which hydrolases may be used in his invention. Note also that Fein teaches topical administration of formulations comprising amidases or ceramidases which are recited as non-elected species in the instant claims.

Additionally, it also would have been obvious to have included a buffer at a pH of about 6, such as a citrate/phosphate buffer, in the Fein enzyme formulation comprising aspartylglucosaminidase (AGA). One of ordinary skill in the art would have been motivated to do this since such a buffer at this pH results in optimal AGA activity, thus ensuring that the AGA is active, which is necessary for the enzyme to act on the skin. Such a buffer at pH of about 6

modifies the environment of the enzyme to one that is favorable to the activation of the enzyme. Since a buffer at pH of about 6 stimulates the activity of AGA compared to buffers at other pHs, the buffer at this pH is an "activator" of AGA. Though Fein indicates that their topically-administered compositions may comprise other compounds "...that either do not affect or only minimally affect the activity of the enzyme," it appears that this is a teaching against compounds that have a negative effect on the enzyme. Clearly, it would be desirable to have an active enzyme, thus an "activator" would have ensured that such is the case.

A holding of obviousness is clearly required.

Applicant's arguments with respect to the rejections of the previously pending claims under 35 U.S.C. 102 and 35 U.S.C. 103 over Meyers, Rudolph-Owen et al., van de Sandt et al., and Martinez, have been fully considered and are persuasive. Therefore, the rejections have been withdrawn. However, upon further consideration, a new ground(s) of rejection is made in view of the Fein and Baumann references.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan E. Fernandez whose telephone number is (571) 272-3444. The examiner can normally be reached on Mon-Fri 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mike Wityshyn can be reached on (571) 272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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